Effective Health Care

Intensity of Surveillance Programs for Patients with Resectable Colorectal Cancer Nomination Summary Document

Results of Topic Selection Process & Next Steps

- The topic area, *Intensity of Surveillance Programs for Patients with Resectable Colorectal Cancer,* was found to be addressed by four evidence-based guidelines and one systematic review. Given that the existing guidelines and systematic review cover this nomination, no further activity will be undertaken on this topic.

Guidelines

- Labianca R, Nordlinger B, Beretta GD, et al. Early colon cancer: ESMO clinical practice guidelines for diagnosis, treatment and follow-up. Ann Oncol Oct 2013; 24 Suppl 6:vi64-72.
- Glimelius B, Tiret E, Cervantes A, et al. Rectal cancer: ESMO clinical practice guidelines for diagnosis, treatment and follow-up. Ann Oncol Oct 2013; 24 Suppl 6:vi81-88.
- Earle C, Annis R, Sussman J, et al. Follow-up care, surveillance protocol, and secondary prevention measures for survivors of colorectal cancer. Toronto, Ontario: Cancer Care Ontario; 2012.
- Cancer Council Australia Colonoscopy Working Party. Clinical practice guideline for surveillance colonoscopy - in adenoma follow-up; following curative resection of colorectal cancer; and for cancer surveillance in inflammatory bowel disease. Sydney, Australia: Cancer Council Australia; 2011.

Systematic Review

- Rose R, Augestad KM, Cooper GS. Colorectal cancer surveillance: What's new and what's next. World J Gastroenterol 2014; 20(8):1887-1897.

Topic Description

Nominator(s): Organization

Nomination Summary: The original nomination focused broadly on imaging procedures for surveillance of resectable breast, colorectal and non-small-cell lung cancers. The scope was narrowed to surveillance of colorectal cancer, based on a preliminary review of the available guidelines on surveillance for the three types of cancer and input from the stakeholder panel that nominated the topic. The guidelines for colorectal cancer contained the most variation and uncertainty in the recommendations.

This nomination focused on the comparative effectiveness of surveillance programs of varying intensities used to monitor for recurrence and new primary tumors in patients

who have undergone treatment for resectable colorectal cancers and have no clinical evidence of disease. “Intensity” within this context consists of the combination of clinic visits and testing (both imaging and non-imaging) and the frequency with which they are carried out. The stakeholder panel members also highlighted the use of 18-fluorodeoxyglucose positron emission tomography (FDG-PET), specifically the hybrid models with computed tomography (PET-CT) as an area of controversy. Because of the differences in guidelines for treatment and surveillance of colon and rectal cancers, separate questions were formulated for these two malignancies.

Staff-Generated PICO for Key Question 1a
Population(s): Patients without clinical evidence of disease after completing primary therapy for resectable colon cancer, at average or elevated risk of recurrence (with separate comparisons for each risk group wherever feasible), undergoing surveillance for recurrence and new primary tumors
Intervention(s): History and physical examination; laboratory tests (e.g., carcinoembryonic antigen [CEA]; imaging procedures (e.g., computed tomography [CT] of the chest, abdomen or pelvis, 18FDG-positron emission tomography [PET] with or without CT, abdominal ultrasound); colonoscopy; sigmoidoscopy
Comparator(s): Different combinations of the above interventions
Outcome(s): Overall survival (OS); disease-specific survival; progression-free survival; time to detection of recurrences, and proportion of recurrences, hepatic metastases, and new primary tumors amenable to curative treatment; changes in treatment plan; health-related quality of life (HR-QoL); harms and costs of follow-up (with separate analyses for subgroups defined by risk of recurrence wherever possible)

Staff-Generated PICO for Key Question 1b
Population(s): Patients without clinical evidence of disease after completing primary therapy for resectable colon cancer, at average or elevated risk of recurrence (with separate comparisons for each risk group where feasible), undergoing surveillance for recurrence and new primary tumors
Intervention(s): More frequent surveillance strategies (i.e., shorter intervals between tests)
Comparator(s): Less frequent follow-up strategies (i.e., longer intervals between tests)
Outcome(s): Overall survival (OS); disease-specific survival; progression-free survival; time to detection of recurrences, and proportion of recurrences, hepatic metastases, and new primary tumors amenable to curative treatment; changes in treatment plan; HR-QoL; harms and costs of follow-up (with separate analyses for subgroups defined by risk of recurrence wherever possible)

Staff-Generated PICO for Key Question 2a
Population(s): Patients without clinical evidence of disease after completing primary therapy for resectable rectal cancer, at average or elevated risk of recurrence (with separate comparisons for each risk group wherever feasible), undergoing surveillance for recurrence and new primary tumors
Intervention(s): History and physical examination; laboratory tests (e.g., CEA); imaging procedures (e.g., CT of the chest, abdomen or pelvis, 18FDG-positron emission tomography (PET) with or without CT, abdominal ultrasound); colonoscopy; flexible or rigid proctosigmoidoscopy
Comparator(s): Different combinations of tests
Outcome(s): Overall survival (OS); disease-specific survival; progression-free survival; time to detection of recurrences, and proportion of recurrences, hepatic metastases, and new primary tumors amenable to curative treatment; changes in treatment plan; HR-QoL; harms and costs of

follow-up (with separate analyses for subgroups defined by risk of recurrence wherever possible)

Staff-Generated PICO for Key Question 2b
Population(s): Patients without clinical evidence of disease after completing primary therapy for resectable rectal cancer, at average or elevated risk of recurrence (with separate comparisons for each subgroup wherever feasible), undergoing surveillance for recurrence and new primary tumors
Intervention(s): More frequent surveillance strategies
Comparator(s): Less frequent follow-up strategies
Outcome(s): Overall survival (OS); disease-specific survival; progression-free survival; time to detection of recurrences, and proportion of recurrences, hepatic metastases, and new primary tumors amenable to curative treatment; changes in treatment plan; HR-QoL; harms and costs of follow-up (with separate analyses for subgroups defined by risk of recurrence wherever possible).

Key Questions from Nominator:

Key Question 1a: For patients with no clinical evidence of disease after treatment for resectable colon cancer, what is the comparative effectiveness of different types of surveillance programs to monitor for recurrence and new primary tumors?
Key Question 1b: For patients with no clinical evidence of disease after treatment for resectable colon cancer, what is the comparative effectiveness of more frequent versus less frequent surveillance programs to monitor for recurrence and new primary tumors?
Key Question 2a: For patients with no clinical evidence of disease after treatment for resectable rectal cancer, what is the comparative effectiveness of different types of surveillance programs to monitor for recurrence and new primary tumors?
Key Question 2b: For patients with no clinical evidence of disease after treatment for resectable rectal cancer, what is the comparative effectiveness of more frequent versus less frequent surveillance programs to monitor for recurrence and new primary tumors?

Considerations

- Colorectal cancer is the third most common cancer in both men and women representing, a significant disease burden in the US. The majority of patients will present with potentially curable disease by surgery with or without adjuvant chemotherapy. However, approximately 30%-50% of patients will develop recurrence.
- The rationale for surveillance in persons after treatment for resectable colorectal cancer is to improve survival by early identification and treatment of cancer recurrence or new primary tumors.
- There is variation in practice in the frequency and type of testing after colorectal cancer treatment. An examination of the available evidence may inform practice and guidelines about surveillance.
- The topic area was addressed by four evidence-based clinical practice guidelines. Although the methods of surveillance covered by each of these guidelines vary, recommendations regarding the testing intervals are similar. However, there is some variation regarding the duration of surveillance.
    - Updated guidelines published in 2013 by the European Society for Medical Oncology (ESMO), one titled, *Early colon cancer: ESMO Clinical Practice Guidelines for diagnosis, treatment and follow-up*, and another titled, *Rectal cancer: ESMO clinical practice guidelines for diagnosis, treatment and follow-up*.

- The colon cancer guideline recommends intensive follow-up, indicating that more intensive surveillance is associated with better overall survival rates compared to minimal or no follow-up. However, the studies the guideline reviewed were heterogeneous in terms of surveillance methods examined, making it difficult to define what constitutes intensive surveillance and to recommend specific surveillance methods. The guideline could only conclude that "more investigations are better than fewer, which in turn are better than no follow-up at all."
- In addition to intensive follow-up, the guideline recommends history, physical examination, and carcinoembryonic antigen (CEA) every 3-6 months for three years and every 6-12 months at years four and five, colonoscopy at year one and every 3-5 years thereafter, and consideration of CT scan of chest and abdomen every 6-12 months for three years for high-risk patients.
- The rectal cancer guideline recommends clinical assessment every 6 months for 2 years and a colonoscopy in the first year.

■ One guideline published in 2012 by Cancer Care Ontario titled *Follow-up care, surveillance protocol, and secondary prevention measures for survivors of colorectal cancer*. It addressed these key questions relevant to the topic
  - Which evaluations (e.g., colonoscopy, CT, CEA, liver function, complete blood count [CBC], chest x-ray, history, physical exam) should be performed for colorectal cancer survivors for surveillance for recurrence of cancer?
  - What is a reasonable frequency of these evaluations for surveillance?
  - The guideline recommends a physical exam, history, and CEA every 6 months for 5 years, abdominal and chest CT scans every year for three years, a pelvic CT scan every year for 3 years if the primary tumor was located in the rectum, and a colonoscopy one year following surgery and every 5 years afterwards as long as the results are normal.

■ *Clinical practice guideline for surveillance colonoscopy - in adenoma follow-up; following curative resection of colorectal cancer; and for cancer surveillance in inflammatory bowel disease* published in 2011 by the Cancer Council Australia.
  - The guideline includes recommendations regarding the effectiveness of and intervals for surveillance colonoscopy following resection for colorectal cancer.
  - It delineates groups of patients who are high risk for recurrence and who may benefit from an increased surveillance frequency. Among these groups of high risk patients are those with Lynch syndrome, those whose diagnoses was made when they were younger than 40 years of age, and those with hyperplastic polyposis and a *BRAF* mutation.
  - It recommends a follow-up colonoscopy for patients who are not high risk should be one year after treatment. Follow-up colonoscopies should be performed at intervals of three (if the peri-operative colonoscopy or one-year colonoscopy finds an advanced adenoma) or five (if results are normal) years.
  - It also recommends that patients with rectal cancer who have undergone a local excision or ultra-low anterior resection may need to be examined additionally using one of the following methods: digital rectal examination, rigid proctoscopy, flexible proctoscopy, and/or rectal endoscopic ultrasound.

■ The topic area was also addressed by a recent systematic review by Rose et al. published in 2014, which provides a synthesis of interim findings from three large surveillance clinical trials – the Follow-up after Colorectal Surgery (FACS) Trial, the Assessment of Frequency of Surveillance after Curative Resection in Patients with Stage II and III Colorectal Cancer (COLOFOL) Trial, and the Gruppo Italiano di Lavaro per la Diagnosi Anticipata (GILDA), as well as other trials, and compares professional society recommendations for surveillance. In addition, the authors discuss innovations relevant to colorectal

cancer surveillance and outline a research agenda aimed to inform a more risk-stratified and personalized approach to follow-up.

- The authors conclude that the accumulation of trial data over the past decades has failed to provide a consistent answer to what surveillance strategies increase the likelihood that recurrences will be caught early and successfully treated thereby prolonging survival. As a result, it is not surprising then that surveillance recommendations also differ considerably across organizations and countries.
- The authors also point out that the large, ongoing colorectal cancer surveillance trials will provide results, which should shed light on effective follow-up for colorectal cancer survivors and provide quality-of-life and economic findings.